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## BLADDER METASTASIS OF RENAL CELL CARCINOMA ; A CASE STUDY

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A 78-year-old man underwent left total nephroureterectomy, and histopathological examination revealed renal cell carcinoma (RCC) of clear cell subtype. Multiple lung metastases were observed, and immunotherapy using IFN- $\alpha$  was introduced after the operation. Gross hematuria was seen 1 year after the operation, and cystoscopy revealed a submucosal tumor in the bladder. Transurethral resection of the tumor was performed, and pathological diagnosis was metastasis from the RCC. Six months later, he died because of multiple metastases of the tumor. Thirty cases of metastasis of RCC to the bladder, including our case, have been reported in Japan.

(Hinyokika Kiyo **53** : 571–574, 2007)

**Key words** : Renal cell carcinoma, Bladder metastasis

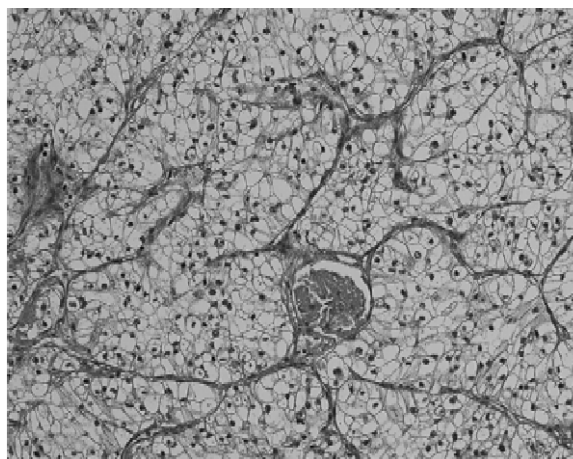
### INTRODUCTION

Metastatic renal cell carcinoma (RCC) in the urinary bladder is uncommon. Usually, it is diagnosed accompanied with widespread disease<sup>1)</sup>. On the other hand, few cases showed solitary metastasis to the bladder and long survival time<sup>2)</sup>. Including our case, 30 cases have been reported in Japan. By summarizing these reports, we discuss the clinical features of metastasis of RCC to bladder.

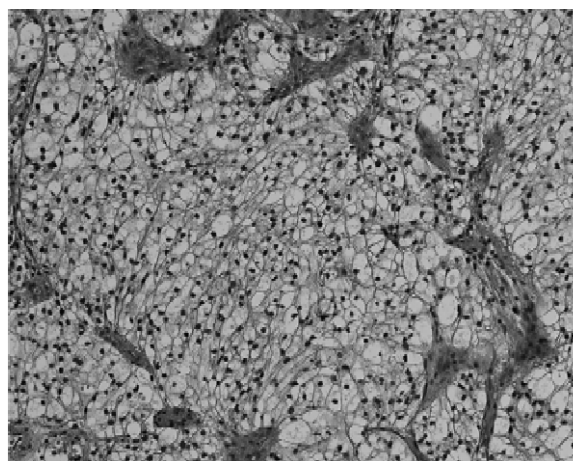
### CASE REPORT

A 78-year-old man visited Yamanashi Prefectural Central Hospital with a history of gross painless hematuria in June 2003. Pyelography showed a defect at the upper calyx of the left kidney, and a poorly enhanced tumor 4 cm in size was seen at the same region on computed tomographic (CT) examination. The tumor showed invasion to the renal parenchyma. From these observations, we suspected renal pelvic cancer, though urinary cytological examination showed class II. Left total nephroureterectomy was performed, and pathological examination revealed RCC of clear cell subtype (Fig. 1A) with metastasis to the adrenal gland of the same site. Chest X-ray showed multiple lung metastases, which indicated stage IV (pT3a, Nx, M1). Immunotherapy using IFN- $\alpha$  was introduced, and complete response was obtained in 6 months. Immunotherapy could not be continued thereafter, because he complained of itching skin following injection.

Gross hematuria was seen 1 year after the operation, and cystoscopy revealed a submucosal tumor 1 cm in size at the posterior bladder wall (Fig. 2). CT scan of the pelvis showed a 1-cm, well-enhanced mass at the same region (Fig. 3). Transurethral resection of the



A



B

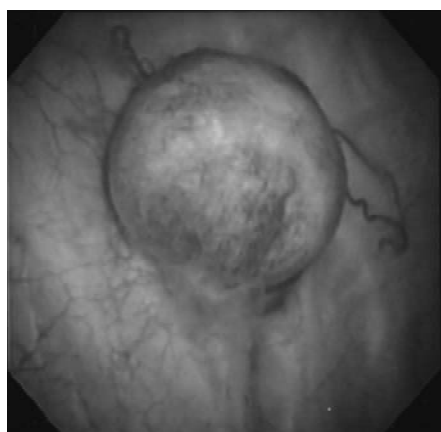
**Fig. 1.** Histopathological finding shows a clear cell carcinoma of the kidney (A). (B) shows a metastatic bladder tumor that is identical to (A).

tumor was performed, and the pathological diagnosis was metastasis of RCC (Fig. 1B). Subsequently, increase in size of lung metastases and multiple bone

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**Table 1.** Time span from the initial diagnosis of renal cell carcinoma (RCC) to the disclosure of bladder metastasis and the existence of metastases to other organs are summarized according to the stage of RCC at the initial diagnosis. TNM system decided in 1997 is applied for stage grouping of RCC.

Stage of RCC at initial diagnosis	Time span to the disclosure of bladder metastasis	Existence of the metastases to other organs
Stage I	5 cases 68 months (36–144 months)	(+) 1 case / (–) 4 cases
Stage II	2 cases 4.5 months (4–5 months)	(+) 1 case / (–) 1 case
Stage III	3 cases 20 months (3–48 months)	(+) 2 cases / (–) 1 case
Stage IV	14 cases 12.7 months (0–108 months)	(+) 10 cases / (–) 4 cases



**Fig. 2.** Cystoscopy shows a submucosal tumor at posterior bladder wall.



**Fig. 3.** CT scan with intravenous contrast medium shows a well enhanced mass at the bladder wall.

metastases were recognized. He died in February 2005.

### DISCUSSION

Common metastatic sites of RCC are lung, lymph node, brain, liver, bone and adrenal gland in decreasing frequency. Metastasis to the bladder is rare. Saitoh examined 1,451 autopsy cases of RCC and 1.6% of them showed metastasis to the bladder<sup>3)</sup>. In Japan, 30 cases of bladder metastasis have been reported. Nineteen cases were male patients and 11 cases were female. Median age of these patients was 56.9 years. Metastasis from the right renal tumor was observed in 18 cases, from the left renal tumor in 10 cases, and the side was not mentioned in 2 cases.

Three different metastatic pathways have been suggested, i.e., hematogenous, lymphatic and metastasis via urinary stream. Hematogenous metastasis can occur through two different paths. One is dissemi-

nation through systemic circulation, and the other is retrograde metastasis through ureteral vein or gonadal vein when the renal vein is obstructed by tumor thrombus<sup>4)</sup>. Metastasis via urinary stream occurs especially when the tumor invades the renal pelvis or after diagnostic biopsy using a ureteroscope<sup>5,6)</sup>. In 6 out of 30 Japanese cases, the lesions of bladder metastasis are around the ipsilateral ureteral orifice, which suggests the seeding implantation of cancer cells. In our case, synchronous adrenal and lung lesions suggest that metastasis occurred through systemic circulation. At the same time, metastasis via urinary stream cannot be ruled out because gross hematuria was seen.

Twenty-four out of 30 cases mentioned the initial stage of RCC. We summarized the time span from the initial diagnosis of RCC to the disclosure of bladder metastasis and the existence of metastasis to other organs according to the stage of RCC at the initial diagnosis (Table 1). In 3 out of 5 cases of stage I, it took more than 5 years before bladder metastasis was disclosed. This indicates that we should not overlook urinary bladder as the site of delayed distant metastasis in the investigation of patients presenting with hematuria after previous nephrectomy. In these cases, solitary metastasis to the bladder is not rare, and if complete resection of metastatic tumor was obtained, prognosis is good thereafter. On the other hand, in most cases of stage IV, bladder metastasis is revealed at the time of initial diagnosis or soon after, and it was accompanied with metastases to other organs, and prognosis is usually poor. There is one exceptional case that showed a 9-year survival, though the initial diagnosis was stage IV with multiple metastases. In this case, immunotherapy using IFN- $\alpha$  and IL-II was introduced together with surgical resection of metastatic tumors. The unique immunobiological behavior and host-cancer relationship are well known phenomena of RCC.

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## 和文抄録

## 腎細胞癌の膀胱転移の1例

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78歳の男性に対し、左腎尿管全摘除術を施行したところ、病理結果は腎細胞癌であった。多発肺転移巣が認められ、IFN- $\alpha$ による免疫療法を開始した。術後1年経過したところで肉眼的血尿が出現し、膀胱鏡検査で粘膜下腫瘍が確認された。経尿道的膀胱腫瘍切除術

を行ったところ、腎細胞癌の膀胱転移であることが分かった。その6カ月後、多発転移により患者は死亡した。これまでに国内では本症例を含め30例の腎癌膀胱転移が報告されている。

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